Dynamic blastomere behaviour reflects human embryo ploidy by the four-cell stage.

Journal: Nat Commun

Publication Year: 2012

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PubMed link: 23212380

Funding Grants: Correlated time-lapse imaging and single cell molecular analysis of human embryo development

Public Summary:
This manuscript reports the first non-invasive diagnosis of human embryo chromosomal abnormalities (genetic abnormalities), based on videotaping the embryos and measuring behavioral changes in the time to divide, fragmentation of cells and other parameters. Results are being translated to clinical applications.

Scientific Abstract:
Previous studies have demonstrated that aneuploidy in human embryos is surprisingly frequent with 50-80% of cleavage-stage human embryos carrying an abnormal chromosome number. Here we combine non-invasive time-lapse imaging with karyotypic reconstruction of all blastomeres in four-cell human embryos to address the hypothesis that blastomere behaviour may reflect ploidy during the first two cleavage divisions. We demonstrate that precise cell cycle parameter timing is observed in all euploid embryos to the four-cell stage, whereas only 30% of aneuploid embryos exhibit parameter values within normal timing windows. Further, we observe that the generation of human embryonic aneuploidy is complex with contribution from chromosome-containing fragments/micronuclei that frequently emerge and may persist or become reabsorbed during interphase. These findings suggest that cell cycle and fragmentation parameters of individual blastomeres are diagnostic of ploidy, amenable to automated tracking algorithms, and likely of clinical relevance in reducing transfer of embryos prone to miscarriage.